REMARKS

Favorable reconsideration of this application as presently amended and in light of the following discussion is respectfully requested.

Claims 1-17 are pending in the present application. Claim 18 was cancelled by a previous amendment. The present Amendment amends independent Claim 1 without introducing any new matter.

In the Office Action, Claims 1-17 were rejected under 35 U.S.C. § 112, first paragraph, as introducing new matter. Claims 1-9, and 11-12 were rejected as unpatentable under 35 U.S.C. § 103(a) over the reference Lindsay et al. (U.S. Patent Publication No. 2004/0238379, hereinafter "Lindsay") in view of Kariyone et al. (U.S. Patent No. 5,242,793, hereinafter "Kariyone"), in further view of Ackley et al. (U.S. Patent No. 6,203,981, hereinafter "Ackley"). Claim 10 was rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone and Ackley, in further view of Hashimoto (U.S. Patent Publication No. 2001/0024788). Claim 13 was rejected as unpatentable under 35 U.S.C. § 103(a) over the reference Lindsay in view of Kariyone and Ackley, in further view of Price (U.S. Patent No. 5,805,014). Claims 14-15 were rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone and Ackley, in further view of Hollis et al. (U.S. Patent No. 5,653,939, hereinafter "Hollis"), Dryja et al. (U.S. Patent No. 5,498,521, hereinafter "Dryja".) and Blackburn (U.S. Patent Application No. 2003/0190608).

Moreover, Claims 14 and 16 were rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone and Ackley, in further view of Hollis et al. (U.S. Patent No. 5,653,939, hereinafter "Hollis"), Sorenson (U.S. Patent No. 5,496,699) and Blackburn. Claim 17 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Lindsay, in view of Kariyone and Ackley, in further view of Anderson et al. (U.S. Patent No. 5,922,591, hereinafter "Anderson"). Claim 18 was rejected under 35 U.S.C. § 103(a) as

being unpatentable over Lindsay, in view of Kariyone, in further view of Heller et al. (U.S. Patent No. 6,281,006, hereinafter "Heller").

In response to the rejection of Applicants' independent Claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly introducing new matter, Claim 1 is amended to delete the reference to the "common gate electrode," and now recites "fixing a potential of the electrolyte solution which covers said active zones with an electrode that applies a gate source voltage to the field effect transistors, the electrode being immerged in said electrolyte solution." Moreover, Claim 1 is also amended to correct minor formal issues. These features are discussed in the specification as originally filed. Applicants' Figure 1 shows an active region 3 between the source S and the drain D of a field effect transistor, and a thin insulation layer 4 is provided on active region 3. (See Specification, p. 5, ll. 23-31.) Moreover, with respect to Figure 1, Applicants' specification recites that "[t]he application of a gate-source voltage U_{GS} between the electrolyte 6 and the source S (for example by means of a single Ag/AgCl electrode E) induces a two dimensional gas of charge carriers at the $Si/Si0_2$ interface, or at the Si/electrolyte interface of each resistor." (Specification, p. 6, ll. 6-12.) The measuring solution 6 covers the gate regions G of the transistors, and the electrode E that is immerged in the electrolyte solution 6 fixes the potential of the electrolyte solution as well as the gate voltage of the transistors, to set the operation point of the sensors that include the transistors. (Specification, p. 7, ll. 10-20.) Accordingly, the features of Applicants' amended independent Claim 1 related to electrode E that applies the gate-source voltage U_{GS} is supported in the disclosure as originally filed, and therefore, Applicants respectfully request reconsideration of the rejection under 35 U.S.C. § 112, first paragraph.

In response to the rejection of Applicants' Claim 1 under 35 U.S.C. § 103(a), Applicants respectfully requests reconsideration of this rejection and traverse the rejection, as discussed next.

Briefly summarizing, Applicants' amended independent Claim 1 is directed to a method for detecting at least one parameter representative of molecular probes fixed to active zones of a sensor, wherein said sensor includes a network of field-effect transistors, each of which has a source region, a drain region, and a gate region which forms one of said active zones on which said representative parameter is detected. The method includes *inter alia* the steps of: bringing some of the active zones into contact with molecular probes in order to fix said probes; bathing at least some of the active zones which have been brought into contact with said molecular probes, in an electrolyte solution; measuring at least one point of at least one of a drain current, source-gate voltage, and source-drain voltage characteristic of at least two of the field-effect transistors, so as to deduce therefrom the representative parameter ***by comparison between at least two measurements obtained for two different active zones*** immerged in the electrolyte solution, and ***fixing a potential of the electrolyte solution which covers the active zones with an electrode that applies a gate source voltage to the field effect transistors***, the electrode being immerged in the electrolyte solution.

Next, the advantages of Applicants' invention over the background art, as shown in Applicants' specification, is next discussed. The features of Applicants' independent Claim 1 allow to make differential measurements between FET transistors that have the same gate voltage, and also have the same voltage for the electrolyte solutions, that allows to substantially increase the sensitivity over conventional differential measurements. By using an electrode E that is located in the electrolyte solution, the voltage of the gates and the electrolyte solution is no longer floating, that reduces noise and artifacts for differential measurements. (See specification at pp. 6-7.) Please note that the above discussion is provided for explanatory purposes only, and is not intended to limit the scope of the claims in any fashion.

Turning now to the applied references, Lindsay is directed to a method for electronically detecting hybridization of a probe nucleic acid and a target nucleic acid, (Lindsay, Abstract) and the reference Kariyone is directed to a selectively permeable membrane that is disposed on an electrode. (Kariyone, Abstract.) However, the pending Office Action confirms that both Lindsay and Kariyone fail to teach the features of Applicants' independent Claim 1 related to the "fixing the potential of the electrolyte solution." (Office Action, p. 7, ll. 1-3.) However, the pending Office Action believes that the reference Ackley teaches such a feature in his Figure 6 and columns 4-5, and assumes that the combination of Ackley with Lindsay and/or Kariyone is proper. (Office Action, p. 7, ll. 4-22.) Applicants respectfully disagree with these assertions, as next discussed.

Independent Claim 1 now requires "fixing a potential of the electrolyte solution which covers the active zones with an electrode that applies a gate source voltage to the field effect transistors, the electrode being immerged in the electrolyte solution." Just like Lindsay and Kariyone, the reference Ackley fails to teach such a feature.

Ackley is directed to a transistor based molecular detection apparatus, configured to detect hybridization of DNA molecules, using a first and a second transistor 73, 74 that are located on a substrate, where the source electrode 75 of the first transistor 73 is electrically couple to the source electrode 76 of the second transistor 74. (Ackley, Abstract, from col. 4, l. 64, to col. 5, l. 5, Fig. 6, col. 2, ll. 51-58.) To perform a molecular detection, a molecule 28 and molecular receptor 16 is bound directly to a surface of the semiconductor channel layer of the first transistor 73. (Ackley, Fig. 1, col. 3, ll. 15-25.) The first transistor 73 is hybridized, while the second transistor 74 will be operated in a non-hybridized state, to form a differential pair of transistors to increase sensitivity of the measurement. (Ackley, col. 4, ll. 53-63, see also col. 2, ll. 32-39.) Moreover, Ackley explains that a binding event is detected by applying a common voltage to gate electrodes 77 and 78, and detecting a difference in

channel currents between the first transistor 73 and the second transistor 74. (Ackley, col. 5, ll. 6-11.) In other words, Ackley applies the same voltage to each gate electrode 77, 78. However, Ackley fails to remedy the deficiencies of Lindsay and Kariyone, because it fails to teach the "fixing a potential" of Applicants' independent Claim 1. In particular, Applicants' Claim 1 requires the fixing of a potential ***of the electrolyte solution which covers the active zones*** with an electrode that applies a gate source voltage to the field effect transistors. This is clearly not the case in Ackley, because he requires that the channels of the transistors 73 and 74 operate in a differential manner. Ackley merely sets the potentials of his two gates to the same voltage level.

Therefore, even if the combination of Lindsay, Kariyone and Ackley is assumed to be proper, the cited passages of the combination fails to teach every element of Applicants' Claim 1. Accordingly, Applicants respectfully traverse, and request reconsideration of this rejection based on these references.

Moreover, the pending Office Action asserts that Ackley teaches the "fixing the potential of the active zones with a common gate electrode." (Office Action, p. 7, ll. 7-8.) This statement is incorrect, because the only potential that is fixed in Ackley's differential transistor measurement device is the gate electrodes 77, 78 themselves, by using a common voltage. Ackley even teaches away from Applicants' Claim 1 features, because Ackley explains that "[b]y burying the gate electrode 84, the source electrode 88, and the drain electrode 90 beneath the channel layer 92, difficulties associated with potential-induced denaturation at the electrodes are prevented." (Ackley, col. 5, ll. 31-34, Fig. 7.) This description of Ackley teaches away from the use of any electrolyte solution that covers the active zones, as required by Applicants' Claim 1, because the channel layer 92 is covered by the drain electrode 90. A reference may be said to teach away when a person of ordinary skill in the art, upon reading the reference, would be discouraged from following the path set

out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Moreover, Applicants respectfully traverse the rejection of his dependent Claim 11. This claim requires a detection of the fixing of the molecular probes to the one of the active zones, as a representative parameter. The pending Office Action asserts that such a feature is taught in the reference Kariyone at his column 17, lines 1-10. (Office Action, p. 6, ll. 1-7.) In addition, the pending Office Action asserts that the combination of Lindsay with Kariyone is proper. (Id., p. 6, ll. 8-21.) Applicants respectfully disagree with these assertions.

Kariyone fails to teach a detection of the fixing of the molecular probes to the one of the active zones, as a representative parameter, as required by Applicants' dependent Claim 11. From column 16, line 45 to column 17 line 8 of Kariyone, the results of an experiment are explained, that lasted for 90 days, where the enzyme electrode is immobilized after preparing a mixed solution and letting it stand for 20 minutes. But nowhere in the reference Kariyone a detection of the fixing of molecular probes is explained or taught.

Consequently, in view of the present amendment, no further issues are believed to be outstanding in the present application, and the present application is believed to be in condition for formal Allowance. A Notice of Allowance for Claims 1-17 is earnestly solicited.

Should the Examiner deem that any further action is necessary to place this application in even better form for allowance, the Examiner is encouraged to contact Applicants' undersigned representative at the below listed telephone number.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Gregory J. Maier
Attorney of Record
Registration No. 25,599

Nikolaus P. Schibli, Ph.D.
Registered Patent Agent
Registration No. 56,994

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/07)
NPS/rct